B. REMARKS

Claims 1, 2, 4, 5, 8, 9, 11-13, 16, 17, 19, 21, 24, 26-28, 30, and 32 stand rejected under 35 U.S.C. 102(b) as being clearly anticipated by Soiffer, et al.

Claims 6, 7, 10, 20, 22, and 31 stand rejected under 35 U.S.C. 103 as being unpatentable over Soiffer, et al. in view of Donnelly, et al.

These rejections are respectfully traversed.

The present invention is directed to methods of inducing a reduced immune response to donor tissue, and of treating a transplant recipient for graft versus host disease. Such reduced immune responses are induced by at least one member selected from the group consisting of isolated fibroblasts and a supernatant from an isolated fibroblast culture.

At Page 3, lines 3-5 of the Final Rejection, the Examiner states that, "'Isolated,' however, can be defined as separated or detached, thus, the fibroblasts need not be purified but only separated form their original source, i.e., the donor's bone."

It is clear that from reading the specification, that when Applicants refer to isolated fibroblasts, they do not mean fibroblasts that merely are removed from the donor's bone or any other tissue where fibroblasts may be present. For example, at Page 7, lines 22-27, the specification states that the fibroblasts can be administered with bone marrow cells or hematopoietic stem cells, which are another group of cells, different from fibroblasts, which have been separated from bone.

> Thus, in the context of bone marrow (hematopoietic stem cell) transplantation, attack of the host by the graft can be reduced or eliminated. Donor marrow can be pretreated with isolated fibroblasts prior to implant of the bone marrow or peripheral blood stem cells into the recipient. The fibroblasts inhibit or reduce the T-cell response such as to reduce or eliminate a recipient from being adversely affected by the donor tissue, i.e., the therapy reduces or eliminates graft versus host response.

(Specification, Page 7, lines 22-27).

Thus, it is clear that Applicants do not intend merely to remove the fibroblasts from bone in that the fibroblasts, which can be one component of bone marrow (or from a source other than bone marrow), are used to treat another component of bone marrow, i.e., hematopoietic stem cells, in order to reduce or eliminate a graft versus host response.

In addition, contrary to the Examiner's assumptions and assertions, the fibroblasts need not be isolated solely from bone marrow. For example, the fibroblasts may be obtained from skin, as indicated at Page 9, lines 24 and 25:

> Although the invention is not limited thereof, fibroblasts can be obtained from skin for use in the methods described herein.

Also, as shown in Example 1, at Page 11, lines 20-22 as follows, the specification provides a working example in which the fibroblasts were obtained from skin:

> Fibroblasts were human normal skin fibroblasts CCD-1087 Sk from 18 years old female obtained from ATCC (Cat # CRL-2104) and were maintained in DMEM – low glucose/10% FCS.

In addition, the present invention also is directed to the use of supernatants derived from fibroblast cultures. Such a supernatant is employed in Example 3.

Therefore, it is clear form the specification of the above-identified application that when Applicants refer to "isolated" fibroblasts, Applicants do more than just separate the fibroblasts form bone or other tissue.

For example, assuming that Applicants can obtain the fibroblasts from bone, it is clear that from reading the specification that the fibroblasts would be separated from other cells in the bone marrow, such as hematopoietic stem cells, before they are employed in the methods of the present invention. For example, it is clear from Page 7, lines 22-27 that the isolated fibroblasts are administered to another isolated group of cells from bone marrow, i.e., hematopoietic stem cells, in order to prevent or reduce or eliminate a graft versus host response.

In addition, the present invention also is directed to the use of supernatants from fibroblast cultures. One skilled in the art would understand that, in order to obtain such

supernatants, one would need to isolate the fibroblasts from other cells, and then culture the isolated fibroblasts in order to obtain the supernatants.

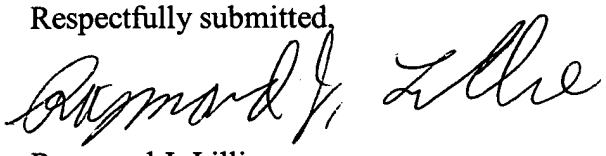
Applicants, in isolating the fibroblasts, clearly undertake steps in addition to the mere removal of a mixture of cells including fibroblasts from bone or other tissue. Thus, when read in the context of the specification, the term "isolated" does not read upon the mere separation of the fibroblasts from bone, as the Examiner asserts.

As stated previously, Soiffer and Donnelly, taken alone or in combination, do not disclose or even remotely suggest to one of ordinary skill in the art that one may administer fibroblasts or a supernatant from an isolated fibroblast culture, in order to induce a reduced immune response against donor tissue, to reduce an immune response against recipient tissue by donor tissue, or to treat a transplant recipient for graft versus host disease. Because the combination of Soiffer and Donnelly does not even remotely suggest Applicants' claimed methods to one of ordinary skill in the art, Soiffer clearly does not anticipate Applicants' claimed methods, and the combination of Soiffer and Donnelly fails to meet the standard for obviousness set by 35 U.S.C. 103.

If a telephone interview would advance prosecution of the above-identified application favorably, the Examiner is invited to contact the undersigned attorney.

For the above reasons and others, this application is in condition for allowance, and it is therefore respectfully requested that the rejections under 35 U.S.C. 102(b) and 35 U.S.C. 103 be reconsidered and withdrawn and a favorable action is hereby solicited.

Respectfully submitted,



Raymond J. Lillie
Registration No. 31,778

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